REMARKS

I. Introduction

Upon entry of the present amendment, claims 1-19 and 21-22 will be pending in this application. Applicants have amended claim 1 to clarify that the controlled-release mechanism provides prolonged delivery of the composition. Support for this amendment appears throughout the specification, particularly at page 16. Applicants have also amended claim 19 to clarify that the claimed composition is delivered in combination with one or more of radiation therapy, phototherapy, surgical resection, immunotherapy, vaccination, interferon treatment, or stereotactic surgery and cancelled claim 20 (previously reciting certain tumor therapies now recited by claim 19).

II. 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 1-22 under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner has indicated that independent claims 1 and 19 state that the moiety "D" can be represented by the group "-CH(O)-" is rendered vague and indefinite because the valencey of the carbon atom is exceeded in for this group. Applicants have amended claims 1 and 19 to remove the bond after the carbohydrate. This was a typographical error and no new matter has been added by its correction.

III. 35 U.S.C. § 103(a)

A. Combination of Ye reference and website articles

The Examiner has rejected claims 1-18 under 35 U.S.C. § 103(a) as unpatentable over Ye et al. in view of four articles entitled:

- "Offering Hope in the Treatment of Brain Cancer," [online], [retrieved on 2002-01-16], retrieved from the Internet <URL:http://www.gliadel.com >
- "A General Description", [online], [retrieved on 2002-01-16], retrieved from the Internet <URL: http://www.alzet.com/products/products-secOl.html >;
- "Duros", [online], [retrieved on 2002-01-22], retrieved from the Internet <URL: http://www.durect.com/wt/durect/page-name/duros>; and
- "The Brain Infusion Kit and Brain Infusion Kit II", [online], [retrieved on 2002-01-16], retrieved from the Internet <URL: http://www.alzet.com/products/products-sec05.html>.

The Examiner states that Ye et al. disclose of the administration of noscapine as an antitumor agent and that the website article entitled "Offering Hope in the Treatment of Brain Cancer" teaches the mode of administering a pharmaceutical as a wafer, the website article entitled "A General Description" discloses osmotic pumps for the administration of pharmaceuticals, the website article entitled "Duros" provides the skilled artisan with the motivation to employ implant technology for the administration of pharmaceuticals to an individual, and that the website article entitled "The Brain Infusion Kit and Brain Infusion Kit II" discloses the administration of pharmaceutically active agents in brain infusion kits.

The Examiner's position is that the claims recite various modes and methods for pharmaceutical administration, such as implantable devices, delivery pumps, wafers, etc. and that it is well within the purview of the skilled artisan to determine dosages, modes and methods of administration. In addition, the Examiner asserts that one having ordinary skill in the art would be motivated to determine optimum amounts as well as modes and methods of administration in order to get the maximum effect of the pharmaceutical agent. Applicants respectfully traverse this rejection and request reconsideration and withdrawal thereof.

First, Applicants note that claim 1 has been amended to clarify that the delivery of noscapine is "prolonged delivery." There is no teaching or suggestion in the Ye reference or any other cited references that prolonged delivery of noscapine can treat neoplastic diseases. Additionally, one of ordinary skill in the art would not be motivated to combine the Ye reference with any of the website articles in order to provide the invention as presently claimed.

The Ye reference describes an experiment designed to treat lymphoid tumors, breast tumors, and bladder tumors. Mice were injected intraperitoneally or intragastrally with noscapine every day for three weeks. There is no suggestion in the Ye reference of a prolonged delivery of noscapine, an alternate delivery method for prolonged delivery of noscapine, nor a suggestion that the delivery methods used were less than optimal or that there was a need for a device or system that could enhance delivery. In other words, there is no motivation to modify the Ye reference as suggested by the Examiner, and accordingly, the Ye reference is not properly combinable with the website articles. Moreover, there is no suggestion in any of the cited references to provide prolonged delivery of noscapine. Accordingly, Applicants respectfully request that this rejection be withdrawn.

B. Combination of Ke reference and website articles

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ke et al. in view of the four articles listed above. The Examiner states that Ke et al. disclose that the alkaloid of noscapine is effective in the inhibition of tumor growth and cites the articles for the propositions outlined above. The Examiner states that the claims recite various modes and methods for pharmaceutical administration, such as implantable devices, delivery

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pumps, wafers and it is well within the purview of the skilled artisan to determine dosages, modes and methods of administration. In addition, the Examiner's position is that one having ordinary skill in the art would be motivated to determine optimum amounts as well as modes and methods of administration in order to get the maximum effect of the pharmaceutical agent. Applicants respectfully traverse this rejection and request reconsideration and withdrawal thereof.

Even if the Ke reference is available to be cited against the claims of this application, there is no motivation to combine the Ke reference with the articles cited. The Ke reference specifically discusses the fact that oral delivery of noscapine is desired. For example, it states "[n]one of the mice that received oral noscapine died, but 30% mortality was found after 2 weeks of treatment with noscapine i.p." and that the results "suggest that oral administration of noscapine is a more tolerable approach than parenteral delivery of the drug." *See* page 220 and 223. This disclosure teaches away from delivering noscapine parenterally because it states that oral delivery is desired.

In order to make out a *prima facie* case of obviousness, the prior art must suggest the desirability of the claimed invention by providing some teaching, suggestion or motivation to combine the references. *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347 (Fed. Cir. 1992). That is not the case here. The reference teaches away from a delivery, other than oral delivery, and does not teach or suggest a prolonged delivery as presently claimed. Accordingly, Applicants respectfully request that this rejection be withdrawn.

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C. The combination of the Ye and Ke references and the Merck Index

The Examiner has also rejected claims 19-22 under U.S.C. § 103(a) as unpatentable over Ye et al. in view of Windholz, M. et al., Editor, The Merck Index, 10th Edition. The Examiner has issued a similar rejection over the Ke reference in combination with the Merck Index. These rejections will be addressed together in this section.

The Examiner states that the Ye and Ke references disclose of the administration of noscapine as an antitumor agent and that Merck Index teaches various antineoplastic and antitumor agents, such as cyclophosphamide, cisplatin, vinblastine, vincristine and vindensine. The Examiner's position is that "[i]t is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose....The idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850 (CCPA 1980). The Examiner asserts that for these reasons, it would have been obvious to one having ordinary skill in the art to modify the prior art teachings by combining these pharmaceuticals, especially when they possess the same utility as antineoplastic agents. Applicants respectfully traverse this rejection and request reconsideration and withdrawal thereof.

The Merck Index describes forms of chemotherapy only. The *Kerkhoven* case addresses the use of compositions that are combined and used for the same purpose. However, the Examiner has not cited any reference that teaches or suggests radiation therapy, phototherapy, surgical resection, immunotherapy, vaccination, interferon treatment, or stereotactic surgery delivered in combination with noscapine. *In re Kerkhoven* does not

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address or consider the situation in which a composition is combined with a surgical *method* or other *process* of treatment. *In re Kerkhoven* addresses the use of compositions that are combined and used for the same purpose.

However, one of ordinary skill in the art would not expect a composition comprising noscapine to be used in connection with a surgical process in order to treat or prevent tumors. Additionally, there is no teaching or suggestion to use noscapine as a preventive measure after surgical excision, as recited by claim 21. In other words, there is no teaching or suggestion of the combination of noscapine in connection with other processes by the prior art. Accordingly, Applicants respectfully request that the Examiner's rejection be withdrawn.

IV. Double Patenting Rejection

The Examiner has rejected claims 1-18 under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,3756,516 in view of articles "offering Hope in the Treatment of Brain Cancer," "A General Description," "Duros," and "The Brain Infusion Kit and Brain Infusion Kit II." The Examiner has also rejected claims 19-22 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,376,516 in view of Windholz, M. et al., Editor, The Merk Index, 10th Edition.

Applicants respectfully traverse this rejection for the above-discussed reasons and request reconsideration and withdrawal thereof. Nonetheless, in the interest of advancing the prosecution of this case, Applicants have also filed a terminal disclaimer in connection with this response, obviating the Examiner's rejection.

CONCLUSION

For at least the above reasons, Applicant respectfully requests allowance of claims 1-22 and issuance of a patent containing these claims in due course. If there remain any additional issues to be addressed, the Examiner is urged to contact the undersigned attorney.

Respectfully submitted,

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